

EXHIBIT B

Application/Control Number: 09/879,480

Page 3

Art Unit: 1634

09/744,675, filed January 29, 2001. Accordingly, priority has not been granted to the stated provisional applications. Furthermore, it is noted that the subject matter of the present claims is entitled to priority only to the instant filing date of June 12, 2001. A claim as a whole is assigned an effective filing date rather than the subject matter within a claim being assigned individual effective filing dates. The priority applications do not disclose the general concept of a method of managing animals by inseminating a female of a species of mammal with an artificial insemination sample having a plurality of spermatozoa wherein at least 90% of said plurality of spermatozoa have a sex determination characteristic corresponding to the same sex of an offspring mammal.

Claim Rejections - 35

USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing bovine offspring wherein the methods comprise inseminating a female bovine with an insemination sample having a plurality of spermatozoa wherein the spermatozoa have been purified to the extent that up to 90% of the spermatozoa have X-bearing chromosomes or wherein up to 90% of the spermatozoa have Y-bearing chromosomes, and while the prior art (Buchanan 2000) has enabled methods of producing equine offspring wherein the methods comprise inseminating a female equine with an insemination sample having a plurality of spermatozoa wherein up

Application/Control Number: 09/879,480
Art Unit: 1634

Page 4

to 90% of the spermatozoa have an X chromosome, and while the prior art (Rens US Patent No. 5,985,216, issued November 16, 1999) has enabled methods of producing porcine offspring wherein the methods comprise inseminating a female porcine with an insemination sample having a plurality of spermatozoa wherein up to 92% of the spermatozoa have an Y chromosome, does not reasonably provide enablement for methods of managing any animal by artificial insemination using an insemination sample having a plurality of spermatozoa wherein up to 100% of the spermatozoa have the same sex determination characteristic and wherein up to 100% male or female offspring are produced. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The claims are drawn broadly to methods of managing an animal by producing a female of a species of mammal, inseminating said female with an artificial insemination sample wherein the sample includes at least 90% of spermatozoa that have the same sex determination characteristic, fertilizing at least one egg of said female and producing an offspring mammal. The claims

Application/Control Number: 09/879,480

Page 5

Art Unit: 1634

further include producing offspring mammals that comprise 90% or more male offspring and 90% or more female offspring.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(l)it is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, specification has not adequately taught one of skill in the art how to practice methods of enriching spermatozoa to purities of 100% in bovine mammals or to purities of 90% or greater in all animals for the following reasons.

The specification at page 6 makes clear that the claimed invention is not intended to be limited to bovine animals. Rather, the claimed invention is applicable "to a variety of species of mammal including, but not limited to, humans, bovids, equids, ovids, canids, goats or swine, as well as less commonly known animals such as elephants, zebra, camels, or kudu...As such, the examples provided are not intended to limit the description of the invention to the management of any particular specie(s) of mammal(s)." Accordingly, Applicant's claims are intended to include the management of human populations by

Application/Control Number: 09/879,480
Art Unit: 1634

Page 6

controlling the sex of offspring, the number of offspring and the size of the population. In particular, claim 14 includes inducing early puberty in a human female; claim 18 includes early weaning of a human; claim 21 includes synchronizing estrous in a human population; claim 23 includes "harvesting said female of said species of mammal" wherein said mammal includes a human. In addition to the clear concerns associated with the harvesting of human beings and the managing of human populations by inducing early puberty in human females, the specification has not enabled the use of such methods in humans. Applicants have not adequately taught any methods of inducing early puberty in a human female and have not taught how a human treated in the above manners could then be used to effectively produce offspring that could be "managed." While the specification states that "Diet is an effective tool to induce puberty" (see page 2), it is not clear as to whether this statement is intended to refer only to bovines. There are no teachings in the specification as to the use of controlling diet as a means of inducing early puberty in human females. Lacking any guidance from the specification as to how one would specifically induce early puberty in a human female and then use this female for reproductive purposes, one of skill in the art would not be able to practice this aspect of the claimed invention. Furthermore, the specification does not make clear as to whether modification of diet so as to cause a specified weight gain induces early puberty in animals other than cattle, such as equine, rabbits, elephants, goats and zebras. The specification does not specifically discuss methods for inducing early puberty in non-bovine animals.

Application/Control Number: 09/879,480
Art Unit: 1634

Page 7

Secondly, the ability to sort sperm from any animal on the basis of a "sex determination characteristic" such that the resulting sample contains more than 90% of sperm having the same sex determination characteristic and to reproducibly generate offspring in which 90% of more of the offspring are male or in which 90% of more of the offspring are female is highly unpredictable. This unpredictability is exemplified by the results set forth in the specification. In particular, pages 40-41 of the specification states:

"Eleven of 16 (69%) calves conceived from semen sorted for X-chromosome were female and all three calves conceived from non-sexed semen were bulls (100%), whereas the only female born to natural serve was female (100%). Seidel et al. (87) reported that 86% of calves conceived from sexed semen are of the desired sex. The result of this data set of 69% of calves conceived from sexed semen were of desired sex, is not an adequate replication of their study as too few individuals were used. The low percent of desired sex was not expected as the true percent of X-chromosome sperm varied from 86-92% for the batches of semen used in the study."

Applicants fail to provide any examples in which semen is sorted to rates above 86-92% and fail to teach how the methodology set forth within the specification could be modified to achieve the production of animals in which more than 69% of the animals of one "desired" sex. The prior art of Rens (US Patent 5,985216, issued 1999) does teach that bovine sperm can be sorted to purities of about 90%. Rens also teaches that under some conditions, porcine sperm could be sorted to a purity of 92% for sperm bearing the Y chromosome. In addition, Buchanan (April 2000, page 1337) teaches methods for sorting equine sperm wherein the sperm were successfully sorted to a purity of 90% for

Application/Control Number: 09/879,480

Page 8

Art Unit: 1634

sperm bearing the X chromosome and to 84% for sperm bearing the Y chromosome. However, there is no specific guidance provided in the specification for how one may accomplish the sexing of sperm to achieve purity rates of 95%, 99% or 100% in bovine animals, in humans or in any other animal. It is unpredictable as to whether one of skill in the art could sort sperm from any animal at purity rates of 90% or above and generate populations of animals in which 90% or more of the offspring are of the same sex. The unpredictability of sorting sperm to high levels of purity, including purity levels above 90% is supported by the teachings in the art. For example, Fugger (1999; cited in the IDS of 6/12/01) teach that using the most current techniques, human sperm cells can be separated to provide samples containing on average 88% enrichment for X-bearing sperm and 69% enrichment for Y-bearing sperm (see page 1439).

Fugger goes on to state that :

"Human sperm cells present unique characteristics that affect the ability to detect and separate X and Y sperm by flow cytometry. The current flow technology appears to be most efficient with sperm cells that have a substantial difference in total DNA, are relatively homogeneous with respect to physical shape and cellular morphology, and are more paddle shaped to take advantage of flow-induced orientation before fluorescence detection. Most human sperm, however, are heterogeneous, vary substantially within and between individuals, are oval in shape, vary in the magnitude of difference in DNA content between X and Y chromosomes due to individual variation in size of the Y chromosome, and contain a relatively small 2.8% difference in total DNA content compared to >3.5% for most domestic animals."

Additionally, Johnson (1992, page 13; cited in the IDS of 6/12/01) teach the difference in DNA content between X and y chromosome bearing sperm for

Application/Control Number: 09/879,480
Art Unit: 1634

Page 9

several organisms, including turkey (0% difference), human (2.9% difference) and rabbit (3% difference). Johnson also reports that rabbit sperm were sorted to purities of 86% for X-chromosome bearing sperm and 81% for Y-chromosome bearing sperm.

However, there are no teachings in the prior art as to how to overcome the problems associated with a lack of difference in the DNA content between X and Y-chromosome bearing sperm or the challenges imposed by the shape, morphology and heterogeneity of sperm. The specification and prior art do not appear to exemplify any methods in which sperm from non-bovine animals are reproducibly purified to 90% or higher purity for both X and Y-chromosome bearing sperm in the majority of species of animals or mammals. The specification does not provide sufficient guidance as to which animal species have sperm which can be sorted to high purity levels and has not taught one of skill in the art what methodologies should be used to sort sperm from non-bovine animals to purity levels of 90% or above. Additionally, the specification does not provide sufficient guidance to enable the skilled artisan to sort sperm from bovine animals to purity levels of 95%-100%. It is unpredictable as to what methodologies should be employed to achieve these high purity levels and to produce offspring in which 90% or more of the offspring are of the same desired sex.

In view of the unpredictability in the art and the lack of specific guidance provided in the specification, undue experimentation would be required to practice the invention as it is broadly claimed.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112: